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Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road,
Wan Chai, Hong Kong, China

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 8011

Title: MOLECULAR PATHOLOGY OF INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS OF THE PANCREAS

Reviewer code: 00159662

Science editor: Ma, Ya-Juan

Date sent for review: 2013-12-11 18:37

Date reviewed: 2013-12-24 13:28

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

1. Section "PATHOLOGY AND CLASSIFICATION OF IPMNs" should be divided in two: (i) Classification, (ii) Pathology 2. The aim should be removed from the section "molecular genetics of IPMNs" and should be transferred to the section introduction. 3. Sub-section "Kirsten ras oncogene": The generalities concerning kras should be removed since it is common knowledge (From "The most frequently... to ...codon 13 (21).). 4. Sub-section "PI3K/Akt" signaling pathway": Only the phrases relative to IPMNs should remain. Notably: "In IPMNs, the frequency of the somatic mutation of the PIK3CA gene is 11%(27). In colorectal cancers, PIK3CA mutations generally arise just before or coincident with invasion(39), while, in IPMNs, seem to be a rather late event on the transition of these lesions to malignancy(27, 42)." 5. Sub-section "BRAF and the RAS/MAPK pathway": Only the phrases relative to IPMNs should remain. Notably: "The rate of the somatic BRAF mutation described for IPMN is only 2.7%(21, 27). The BRAF mutation frequency is then low compared with those observed in malignant melanoma and colon cancers, but anyway the alteration of the Ras-Raf-MEK-ERK-MAP kinase pathway by BRAF mutation together with Ras mutation may play an important role in the tumorigenesis of IPMNs(21, 27); it is possible that tumors with both BRAF and KRAS mutations have an accelerated course in the development or progression(27)." 6. Sub-section "Telomerase Reverse Transcriptase Expression": The generalities about telomerase should be removed. Notably from "Human telomeres are... to ... the pancreatic ones(54)." 7. Sub-section "Hedgehog signaling pathway": The generalities should be removed, From "The Hedgehog family... to ... and in its precursor lesions(62)." 8. Sub-section "Cyclin-dependent kinase inhibitor 2A/p16": The generalities should be removed from "CDKN2A is... to ... pancreatic carcinogenesis." 9.



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Sub-section "TP53 gene": The generalities should be removed from "The tumor suppressor... to ...hepatocellular cancer(78)." 10. Sub-section "Deleted in Pancreatic Cancer locus 4 (DPC4)". The generalities should be removed from "DPC4 tumor-suppressor gene... to ...of the cases)(84, 86, 87)." 11. Sub-section "Serine/threonine kinase 11 gene (STK11)". The generalities from "STK11 gene... to ...various neoplasms(93, 94)." should be removed. 12. Sub-section "Brahma-related gene 1". Introductory phrases should be removed from "BRG1, encoded... to ...pancreatic cancer(101)." 13. Sub-section "The S100 protein family". a. Introductory phrases from "The members of the... to ...survival and invasion(117)." Should be removed. b. The following phrases should be removed "From Protein S100A4... to pancreatic carcinomas(124)." c. The following phrases should be removed "from Protein S100A11... to ...prostate cancer(130)." 14. Sub-section "Aberrant expression of microRNAs" a. The generalities concerning microRNAs should be removed from "microRNAs(miRNAs) are... to ...leukemia(143)." b. The part of the text "From chromosome 17q23.2... to...pro-apoptotic(152)." Should be removed c. The phrases from "miRNA-217 is a tumor... to ...and HOXB3(159, 160)." Should be removed as irrelevant 15. Sub-section "Human Mucin genes expression" a. The generalities from: "MUCs are a group... to ...in ductal adenocarcinoma." Should be removed



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ESPS Manuscript NO: 8011

Title: MOLECULAR PATHOLOGY OF INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS OF THE PANCREAS

Reviewer code: 01204006

Science editor: Ma, Ya-Juan

Date sent for review: 2013-12-11 18:37

Date reviewed: 2014-01-01 05:22

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> [Y] Accept
<input type="checkbox"/> [Y] Grade B (Very good)	<input type="checkbox"/> [Y] Grade B: minor language polishing	<input type="checkbox"/> [] Existed	<input type="checkbox"/> [] High priority for publication
<input type="checkbox"/> [] Grade C (Good)	<input type="checkbox"/> [] Grade C: a great deal of language polishing	<input type="checkbox"/> [] No records	<input type="checkbox"/> [] Rejection
<input type="checkbox"/> [] Grade D (Fair)	<input type="checkbox"/> [] Grade D: rejected	BPG Search:	<input type="checkbox"/> [] Minor revision
<input type="checkbox"/> [] Grade E (Poor)		<input type="checkbox"/> [] Existed	<input type="checkbox"/> [] Major revision
		<input type="checkbox"/> [] No records	

COMMENTS TO AUTHORS

This is a comprehensive overview that covers virtually every relevant molecular event known to date pertaining to IPMN. I encourage the authors to use some of the information listed in Table 3 to construct a practical diagnostic algorithm that integrates imaging and histologic findings and help guide practicing pathologists fine-tune their classifications of real-life cases.



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Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 8011

Title: MOLECULAR PATHOLOGY OF INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS OF THE PANCREAS

Reviewer code: 00039635

Science editor: Ma, Ya-Juan

Date sent for review: 2013-12-11 18:37

Date reviewed: 2014-01-13 19:50

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

It's an interesting overview on IPMNs' molecular characteristics. I'd cut some of the introduction in the sub-sections when you describe general characteristics of the genes you describe in your paper. What about your personal experience: even if it's a review, on my personal opinion your team personal approach after histological diagnosis could be very interesting resulting in more strength of the paper.



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Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 8011

Title: MOLECULAR PATHOLOGY OF INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS OF THE PANCREAS

Reviewer code: 00672164

Science editor: Ma, Ya-Juan

Date sent for review: 2013-12-11 18:37

Date reviewed: 2014-01-20 11:14

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
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<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

In this review article, the authors summarized various genetic and epigenetic alterations identified in intraductal papillary mucinous neoplasm (IPMN). Given the recent advancement of imaging studies and recognition of the disease, IPMN is increasingly diagnosed especially in elderly patients. Thus, differentiation of high-risk tumors that warrant surgical intervention from low-risk tumors that can be non-surgically followed has become important, and understanding the molecular alterations associated with IPMN, especially those associated with high-risk lesions, may help risk stratification. With this background, this review is potentially interesting. Unfortunately, however, it lists genetic and epigenetic alterations reported in IPMN in a random fashion (irrespective of their prevalence and significance in malignant transformation). It is worth reorganizing the contents to emphasize alterations that are significant in the differentiation of: 1. IPMN vs. other pancreatic cystic neoplasms; 2. high-risk vs. low-risk IPMN lesions. In addition, if the authors could come up with recommendations on a panel of molecular assays that differentiate those lesions, it would be very helpful. Of different note, the manuscript may need professional editing by a native English speaker.

Minor issues 1. page 6: moderate -> intermediate-grade 2. page 7: Colloid carcinoma is not a common lesion in the skin. 3. Page 7: The oncocytic type is by definition of high-grade dysplasia based on its architectural complexity, but it may not be so proliferative. 4. Pages 25-26: MUC5AC expression is a hallmark of IPMN, and thus, it is seen all IPMN lesions irrespective of histologic grades and epithelial subtypes.